

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB2004/003096

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 C07K14/82 C12N9/12

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>HAWLEY S A ET AL: "Characterization of the AMP-activated protein kinase kinase from rat liver and identification of threonine 172 as the major site at which it phosphorylates AMP-activated protein kinase."</p> <p>THE JOURNAL OF BIOLOGICAL CHEMISTRY. 1 NOV 1996, vol. 271, no. 44, 1 November 1996 (1996-11-01), pages 27879-27887, XP002315194 ISSN: 0021-9258 the whole document</p> <p>-----</p> <p>-/--</p>	<p>1-7, 11-19, 22,23, 30,32, 33,37-39</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

28 January 2005

Date of mailing of the international search report

28. 04. 2005

Name and mailing address of the ISA

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE WPI Section Ch, Week 200222 Derwent Publications Ltd., London, GB; Class B04, AN 2002-171818 XP002315199 & WO 02/06520 A1 (CHUGAI RES INST MOLECULAR MEDICINE INC) 24 January 2002 (2002-01-24) the whole document -& WO 02/06520 A1 (CHUGAI RES INST MOLECULAR MEDICINE INC) 24 January 2002 (2002-01-24) -----	1
X	BAAS A F ET AL: "Activation of the tumour suppressor kinase LKB1 by the STE20-like pseudokinase STRAD" EMBO JOURNAL, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 22, no. 12, 16 June 2003 (2003-06-16), pages 3062-3072, XP002298130 ISSN: 0261-4189 the whole document -----	28,29
A	BOUDEAU J ET AL: "LKB1, a protein kinase regulating cell proliferation and polarity" FEBS LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 546, no. 1, 3 July 2003 (2003-07-03), pages 159-165, XP004433636 ISSN: 0014-5793 the whole document -----	
A	NATH NANDITA ET AL: "Yeast Pak1 kinase associates with and activates Snf1." MOLECULAR AND CELLULAR BIOLOGY. JUN 2003, vol. 23, no. 11, June 2003 (2003-06), pages 3909-3917, XP002315195 ISSN: 0270-7306 the whole document -----	
A	BEAULOYE^A^ ^B C ET AL: "Insulin antagonizes AMP-activated protein kinase activation by ischemia or anoxia in rat hearts, without affecting total adenine nucleotides" FEBS LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 505, no. 3, 21 September 2001 (2001-09-21), pages 348-352, XP004309604 ISSN: 0014-5793 the whole document ----- -/--	

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>HAWLEY SIMON A ET AL: "Complexes between the LKB1 tumor suppressor, STRAD alpha/beta and M025 alpha/beta are upstream kinases in the AMP-activated protein kinase cascade." JOURNAL OF BIOLOGY (ONLINE) 2003, vol. 2, no. 4, 24 September 2003 (2003-09-24), page 28, XP002298131 ISSN: 1475-4924 the whole document</p>	<p>1,4-6, 15-23, 28-30, 32,33, 37-39</p>
P,X	<p>SHAW R J ET AL: "The tumor suppressor LKB1 kinase directly activates AMP-activated kinase and regulates apoptosis in response to energy stress" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 101, no. 10, 9 March 2004 (2004-03-09), pages 3329-3335, XP002298134 ISSN: 0027-8424 the whole document</p>	<p>1,24,25, 28-30, 32,33, 37-39</p>
E	<p>WO 2004/113562 A1 (MEDICAL RES COUNCIL [GB]; UNIV COLUMBIA [US]; CARLING DAVID [GB]; WOOD) 29 December 2004 (2004-12-29)</p> <p>the whole document</p>	<p>1-3,7,9, 11,12, 14-16, 18,20, 21,23, 32,33</p>
T	<p>BOUDEAU JÉRÔME ET AL: "M025alpha/beta interact with STRADalpha/beta enhancing their ability to bind, activate and localize LKB1 in the cytoplasm." THE EMBO JOURNAL. 1 OCT 2003, vol. 22, no. 19, 1 October 2003 (2003-10-01), pages 5102-5114, XP002315196 ISSN: 0261-4189 the whole document</p>	
T	<p>HONG SEUNG-PYO ET AL: "Activation of yeast Snf1 and mammalian AMP-activated protein kinase by upstream kinases." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA. 22 JUL 2003, vol. 100, no. 15, 22 July 2003 (2003-07-22), pages 8839-8843, XP002315197 ISSN: 0027-8424 the whole document</p>	

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	<p>SUTHERLAND CATHERINE M ET AL: "Elm1p is one of three upstream kinases for the Saccharomyces cerevisiae SNF1 complex." CURRENT BIOLOGY : CB. 5 AUG 2003, vol. 13, no. 15, 5 August 2003 (2003-08-05), pages 1299-1305, XP002315198 ISSN: 0960-9822 the whole document</p>	
T	<p>WOODS A ET AL: "LKB1 is the upstream kinase in the AMP-activated protein kinase cascade" CURRENT BIOLOGY, CURRENT SCIENCE., GB, vol. 13, no. 22, 11 November 2003 (2003-11-11), pages 2004-2008, XP002298132 ISSN: 0960-9822 the whole document</p>	
T	<p>LIZCANO J M ET AL: "LKB1 is a master kinase that activates 13 kinases of the AMPK subfamily, including MARK/PAR-1" EMBO JOURNAL, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 23, no. 4, 25 February 2004 (2004-02-25), pages 833-843, XP002298133 ISSN: 0261-4189 the whole document</p>	
T	<p>HARDIE D G: "THE AMP-ACTIVATED PROTEIN KINASE PATHWAY - NEW PLAYERS UPSTREAM AND DOWNSTREAM" JOURNAL OF CELL SCIENCE, CAMBRIDGE UNIVERSITY PRESS, LONDON, GB, vol. 117, no. PART 23, 2004, pages 5479-5487, XP008040901 ISSN: 0021-9533 the whole document</p>	

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## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-25,28-30,37-39 completely, and claims 32 and 33 partially

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

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### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-25,28-30,37-39 completely, and claims 32 and 33 partially

1.1. claims: 1-25,30 completely, and claims 31-32 partially

An LKB1 complex comprising STRAD and M025, preparation thereof, and its use in the identification of modulators of its phosphorylation of AMPK.

1.2. claims: 28,29

Method for identifying patients with PJS or an increased susceptibility thereto by analysing the STRAD and/or M025 genes for mutations.

1.3. claims: 37-39

AMPK subfamily members with a mutation replacing Thr172 and nucleic acids encoding them  
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2. claims: 26,27

Method for identifying binding partners of M025.  
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3. claims: 31 completely, and claims 32 and 33 partially

Use of an AMPK subfamily member in the manufacture of a medicament for treating diabetes or obesity.  
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4. claims: 34-36

Peptide substrates for LKB1 and antibodies reactive therewith  
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# INTERNATIONAL SEARCH REPORT

Information on patent family members

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Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 0206520	A1	24-01-2002	AU	7106701 A		30-01-2002
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WO 2004113562	A1	29-12-2004	GB	2402938 A		22-12-2004
			US	2005026233 A1		03-02-2005
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